Modern Concepts of Cardiovascular Disease

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PRE-HARVEIAN CONCEPTS OF THE CIRCULATION

The development of the modern concept of the circulation of the blood may well be started with a review of the thoughts of Galen (129-201 A.D.). The Galenic scheme of the circulation, in short, was as follows: That the nutrient blood was derived from the liver and distributed through the vena cava and the veins to the body. The right heart received blood by means of diastolic aspiration, one part going through the invisible pores of the septum into the left ventricle, the other, through the pulmonary artery to the lungs, partly to serve for nutrition, partly to be mixed with air. Perhaps Galen thought too of a blood current through the lungs and to the left ventricle. From the left ventricle blood was expelled by means of the aorta throughout the whole body. The nutrition of the heart took place through the coronary vein. But in order that the lungs might receive blood from the left ventricle (the existence of the bronchial arteries was not known), he postulated a physiological regurgitation through the bicuspid valves.

Galen gave the experimental proof that the arteries contained blood and nothing but blood: first, he showed that upon puncturing an artery, blood immediately emerged; second, when an artery was ligated in two proximate places, the portion between was found to be filled with blood. He furthermore demonstrated by tapping the left ventricle in animals that it contained blood and not, as formerly believed, an aeriform substance.

He gave a correct description of the four valves of the heart and stated: "It seems that all these valves have a common function in preventing regurgitation, appropriate to both directions, one set leading away from the heart and preventing return by that route, the other leading into the heart and preventing escape from it."

Galen described the communication between the arterial and venous systems: "There is generally a mutual anastomosis or joining of the arteries and veins, and they transfer blood and spirit equally from each other by invisible and very small passages." Both Aristotle and Hippocrates were ignorant of this reciprocal relationship. As to the postulated interventricular communication, it should be borne in mind that he spoke of "those openings so tiny that they escape inspection," and Vesalius, though already doubtful, still used almost the same words. As to the postulated bronchovascular communication (needed for the admixture of air with the blood), Galen thought that they were so minute that air might pass to the blood, but not vice versa; although this, he most interestingly added, happened in the presence of cough with hemoptysis.

He performed the famous experiment (later to be repeated by Fabrici d'Aquapendente, Andrea Cesalpino and William Harvey) of bringing into prominence the veins of the forearm by bandaging the arm above the cubital fossa; and remarked that the jugular veins became conspicuous upon screaming and forced expiration.

The following observations were of special interest in regard to the lesser circulation: He noticed in the animal the distension of the pulmonary artery (then called vena arteriosa) upon contraction of the heart and stated that this vessel pulsated like an artery and, structurally, was an arterial vessel. The hypothesis that the pulmonary veins carried only aeriform spirits was combatted by arguing how much simpler it then would have been for nature to anastomose the bronchi with the left heart. And he reasoned that if the pulmonary artery would serve only to nourish the bronchial system, why would not a very small vessel suffice, while actually we are dealing with a large and conspicuous vessel.

Two passages indicated perhaps that Galen thought of the existence of a current through the lesser circulation: "There is only but one way from the lung to the heart." And, when speaking of the anastomoses between the arteries and veins in the lungs, he said that the blood was "transferred into the arteries."

No further progress was made until the thirteenth century.

Ibn An-Nafis (thirteenth century) lived in Cairo, Egypt. This Arabian physician, without knowledge gained from dissection (for he stated in a preface: "The interdiction of the religious law and our own natural charity have prevented us from practical dissection"), gave a description of the theory of the lesser circulation. He said in his commentary on the anatomy in the Canon of Ibn Sina: "But there is no passage between these two cavities; for the substance of the heart is solid in this region and has neither a visible passage, as was thought by some persons, nor an invisible one which could have permitted the transmission of blood, as was alleged by Galen. The pores of the heart are closed and its substance is thick. Therefore, the blood, after having been refined, must rise in the arterious vein to the lung in order to expand in its volume and to be mixed with air so that its finest part may be clarified and may reach the venous artery in which it is transmitted to the left cavity of the heart . . ." "There exist perceptible passages (or pores) between the two (blood vessels)."

The middle of the sixteenth century was reached in Europe before Vesalius had written his great anatomy. One of his physiological contributions was the use of artificial respiration for animal experimentation by the introduction of a canula into the trachea. This was described in the last book of his De vivi sectione nonnulla and preceded Robert Hooke's presentation to the Royal Society (On Preserving Animals Alive, 1667) by one and one-half centuries. It permitted him to study, for a prolonged period, the pulsatory movements of the heart.

The lesser circulation was again described by Miguel Servetus as well as by Realdo Colombo. It is possible, though improbable, that Servetus knew of Ibn An-Nafis' work, although his passage read like an extract from it. Servetus studied medicine in Paris but did not return to Spain. It is also possible that he learned the idea either when he was in

Padua, or from the Spanish physician Valverde, a pupil of Colombo. The latter's anatomy was not published until 1559, the year of his death, and he stated in the preface that the manuscript had been finished for several years. He well may have been teaching his ideas for many years prior to its publication, but it is also possible that Colombo obtained his knowledge from Servetus. While the latter's treatise was published in 1553 (and although practically the entire edition was burned, a few copies escaped), it was ready in manuscript form long before that time. We know that he sent it to a friend in Padua in 1546 where Colombo may have seen and studied it. Of course, it is reasonable to assume that their descriptions were given independently of each other.

Servetus inserted the passage in question in his theological work, Restitutio Christianismi, in order to prove the accurateness of the biblical dictum that the soul is in the blood. He still considered that perhaps the septum might be permeable, and then stated that the blood was driven by a long passage through the lungs; here it was mixed with air and was finally attracted by the left ventricular diastole; the brighter color of the blood was attributed to the process in the lungs.

Servetus stated that his findings differed from those of Galen but he referred only to books six and seven of his De usu partium and those contained only a part of Galen's doctrines.

Colombo was the first to point out the function of the atria, i.e., during ventricular systole, to collect the affluent blood. He also insisted on the absolute impermeability of the interventricular septum. In book seven and eight of his De re anatomica he said in regard to the pulmonary veins: "If you will inspect it not only in the cadavers but in the living animal, you will find it filled with blood in all of them." And: "The blood is carried by the pulmonary artery to the lungs, here it is made thin, and is carried, mixed with air, through the pulmonary vein to the left ventricle."

Neither Servetus nor Colombo spoke of the small anastomosing vessels.

Ibn An-Nafis, Servetus and Colombo adhered to the Galenic doctrine that only a part of the right ventricular blood flows through the lungs in order to be altered into the spiritus vitalis. The other part flows distally into the veins. These three authors, therefore, have not described the pulmonary circulation in Harvey's sense, i.e., that *all* blood passes the lungs.

It was Guilio Cesare Arantio, professor of medicine and anatomy in Bologna, who refuted the passage of blood through the interventricular septum on the basis of physiological reasoning. He stated, in his Observationes Anatomicae, published in 1587, that it would be impossible for the greater part of right ventricular blood to be pressed through the invisible pores of this compact tissue during the short duration of systole. Secondly, why should the right-sided blood (thought at those times to be the thicker) shift towards the left-sided blood (thought to be the thinner)?

The venous valves and their function were described by three individuals in particular prior to the time of Harvey, namely, Fra Paolo Sarpi, Giovanni Battista Canana and Girolamo Fabrizi d'Aquapendente (De venarum ostiolis, 1574); the latter is the successor to Faloppio in Padua, and the teacher of William Harvey.

A man of special importance in the history of the circulation was the great Latin genius, Andrea Cesalpino (1519-1603), who assisted Vesalius in 1543 and taught botany and medicine in Pisa, where he was the director of the botanical garden. Later he was professor in Rome. Our citations will refer to two of his treatises only, namely, to the fifth book of his Quaestiones peripateticae, published in Florence in 1569, and to the second book of his Quaestiones medicae, published in Rome in 1595.

The following passages should prove that he correctly understood and described the anatomic-hydraulic features of the general circulation and for the first time introduced the term circulation. It should be remembered that at his time the microscope had not been invented.

When he spoke of the passage of blood, he spoke of capillaries; for instance: "The distal portions of the veins end in tiniest split capillaries." As to the blood flow in the vessels, he said: "The blood flows from the arteries into the veins." And: "The blood flows towards the heart."

In order to prove that the veins carry blood toward the heart, he argued in the following fashion: "But the following matter seems worthy of consideration, the reason why veins when ligatured swell on the far side and not on the near side of the ligature. This is a fact well known by experience to those who let blood: for they place the ligature on the near side of the place of incision, not on the far side, because the veins swell on the far side, not on the near side of the ligature. But exactly the contrary ought to happen if the movement of the blood and the spirits took place in the direction from the viscera to all parts of the body."

He correlated the robust wall of the arteries with the higher inside pressure, and the following passage sounds very modern indeed: "The strength of animals goes with a moderate degree of (blood) pressure. With the very peripheral portions of the vessels widened, the blood stream would flow easier, but then the vessels are relaxed excessively: those, for instance, who stay too long in a hot bath go into a collapse. Quite a tension would result if those vessels were much constricted; but this would bring about the danger of impending suffocation, because these vascular pathways would not permit the blood to flow forth adequately."

The interrelation of heart and blood vessels was described as follows: "The movement in the vessels is caused by the heart, but they are not the cause of the heart's movement proper;" and: "When the heart contracts, the arteries are dilated, and when it is dilated, they are constricted."

And finally, two famous passages: "Blood flows from the veins into the heart, from the heart into the arteries, this being the only open pathway because of the position of the valves." And: "The passages of the heart are so arranged by nature that from the vena cava a flow takes place into the right ventricle, whence the way is open into the lung. From the lung moreover, there is another entrance into the left ventricle of the heart, from which then a way is open into the aorta, certain membranes being so placed at the mouths of the vessels that they prevent return. Thus there is a sort of perpetual movement from the vena cava through the heart and lungs into the aorta."

It remained for the great synthetic mind of Harvey to go beyond scientific theory and to methodically and experimentally give the proof.

Appropriate to these pre-Harveian conceptions are the words of Sir Michael Foster who was so much interested in the history of physiology.

"To whom shall be given the honour of a discovery? This question can never be answered fully; science is a continuous process, each investigator must of necessity build on the work of those who came before him. What we know and what we think is a stream which flows by us and through us, fed by the far-off rivulets of long ago."

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